REMARKS

Claims 1-35 are pending in the application. Claims 1, 2, 7, 9-11, 13-15, 17, 19, 20, 23, 26, and 30-35 have been cancelled by this amendment. New claims 36-39 have been added to the application. Therefore, claims 3-6, 8, 12, 16, 18, 21, 22, 24, 25, 27-29, and 36-39 are at issue. Claims 30-35, directed to a nonelected invention, have been cancelled without prejudice to filing a continuing application directed to the subject matter of these claims.

Claim 27 has been amended to incorporate the features of original claim 1 into claim 27 to more distinctly claim the lipid emulsion composition. Claims 3-6, 8, 12, 16, 18, 21, 22, 24, and 25 have been amended to recite a method, and to directly or ultimately depend from method claim 27. Claims 28 and 29 have been amended to correct the pendency of these claims.

New claims 36-39 recite various toxins removed from the blood stream by the method of the present invention. Support for new claims 36-39 can be found in the specification at page 3, lines 1-3 and page 6, lines 7-26.

Claims 1-29 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In view of the amendments to the claims, it is submitted that this rejection has been overcome. In particular, claims 2 and 23 have been cancelled, which eliminates confusion between the terms "surfactant" and "emulsifier." Cancellation of claim 2 also eliminates confusion with respect to the presently claimed tonicity

modifiers. The dependency of claims 28 and 29 has been corrected. Accordingly, the rejection of the claims under 35 U.S.C. §112, second paragraph, has been overcome and should be withdrawn.

Claims 1-26 and 28 stand rejected under 35 U.S.C. §102(b) as being anticipated over cited references. In view of the amendments to the claims which cancel composition claims or convert composition claims into method claims, it is submitted that these rejections are moot. With respect to claim 28, it is assumed that this claim was included in the rejection because it erroneously depended from a compound claim. Claim 28 now properly depends from method claim 27.

Claims 27-29 stand rejected under 35 U.S.C. §103 as being obvious over Asher et al. U.S. Patent No. 4,183,918 ('918), alone or in combination with Takami et al. U.S. Patent No. 4,323,563 ('563) and Hope et al. U.S. Patent No. 6,139,871 ('871). For the reasons set forth below, it is submitted that this rejection should be withdrawn.

The present invention is directed to a method for removing a toxin from the circulation by *intravenously* infusing a lipid emulsion composition as recited in claim 27. The lipid emulsion composition can be infused at an initial rate, then at a steady state rate, as recited in claim 29. In the claimed method, the toxin permeates the lipid emulsion composition and is withdrawn from the bloodstream. The toxin-permeated lipid emulsion composition then is slowly metabolized, which releases the toxin slowly and allows a safe detoxification. See specification page 6, line 27 through page 7, line 5. The method is effective, for

example, in removing anesthetic agents, such as bupivacaine and lidocaine, and other toxins from the bloodstream (specification, page 3, lines 1-3 and page 6, lines 7-12).

In particular, the present method is directed to removing "external" or "acute" toxins from the bloodstream, i.e,. toxins that are "poisonous or noxious agents present in the circulation" (specification, page 4, lines 2-5) and that are administered purposefully or accidentally to an individual. Also see specification, page 6, lines 7-26. The present method is *not* directed to removing "chronic" or "latent" toxins, such as cholesterol, that accumulate in the body by natural or life-style processes. In fact, applicants teach that cholesterol can be used as an *ingredient* of the lipid emulsion composition (see specification, page 3, line 15) to help eliminate toxins from the bloodstream.

The cited '918 patent discloses medicinals for *ingestion* that may be utilized as traps for toxins present in the *gastrointestinal* (GI) system, or as slow-release compositions for drugs. The medicinals are designed to be stable during passage through the GI tract. The '918 patent at column 4, lines 5-65 teaches uses of the disclosed compositions, and that because compositions typically are "broken in the stomach," the '918 compositions must be inert to the stomach environment. The '918 patent fails to teach or suggest the use of *any* composition to remove toxins from the bloodstream or the use of an *intravenous* application of the composition.

The environments in the bloodstream and the stomach are so diverse that persons skilled in the art are well aware that a composition suitable for ingestion is not necessarily suitable for intravenous administration, and vice versa. Furthermore, the toxins present in the bloodstream (to which the present invention is directed) are substantially different from toxins found in the GI system, e.g., an anesthetic (bloodstream) vs. the ammonia, phenol, phosphate, and metal toxins of Table 2 of the '918 patent (GI). The '918 patent fails to teach or suggest that the composition disclosed therein can remove toxins from the bloodstream, or that the composition can even be administered into the bloodstream.

In summary, the '918 patent simply contains no teaching or suggestion that would lead a person skilled in the art, after reading the '918 patent, to consider using a lipid emulsion designed for *ingestion* and the removal of *GI* toxins to remove toxins from the bloodstream by an intravenous administration of the composition. There is no incentive for a person skilled in the art to alter the teachings of the '918 patent in such a way because no reasonable expectation of success exists, e.g., the substantial differences between the GI system and bloodstream environments and the substantial differences between the toxins present in the stomach and the bloodstream.

The disclosures of the secondary '563 and '871 patents fail to overcome the deficiencies of the primary '918 reference. The '563 patent merely teaches a specific emulsifier for preparing fat emulsions for ingestion. The emulsifier avoids hemolytic action and

is an improvement over the egg yolk and soybean phospholipids used in the prior art.

The '563 patent does not teach or suggest that the emulsifier can be used in a composition to remove toxins from a bloodstream, and does not add anything to the teachings of the '918 patent with respect to removing toxins from a bloodstream.

Persons skilled in the art arguably may consider using an emulsifier of the '563 patent in a composition of the '918 patent, but the combination of references still does not teach or suggest a method of removing toxins from circulation for the reasons set forth above with respect to the nonobviousness of the claims over the '918 patent. In summary, the '918 patent is directed to removing GI toxins by oral administration of an emulsion, and the '563 patent is directed to an emulsifier for fat emulsions with *no* teachings of what the fat emulsions accomplish. The '563 patent solely is directed to an improved emulsifier for a fat emulsion, which overcomes the problem of prior emulsifiers (e.g., vomiting, diarrhea, and anemia). Like the '918 patent, the '563 patent fails to teach or suggest the removal of toxins from the bloodstream by an intravenous administration of a lipid emulsion composition.

The '871 patent is directed to a composition and method of treating atherosclerosis. The teachings of the '871 patent are substantially different from the presently claimed methods. The present claims are directed to removing acute, externally administered toxins from the bloodstream, as opposed to latent, internally derived, toxins (e.g., cholesterol), as de-

scribed above. In fact, as stated above, a component of a lipid emulsion composition utilized in the present invention *can be* cholesterol. The '871 patent fails to teach or suggest the removal of *acute* toxins from the bloodstream, or to teach or suggest a composition as presently recited in the claims to remove acute toxins from the bloodstream.

In summary, the primary '918 patent is directed to removing *different* toxins from a *different* system of the body by administering an emulsion *via* a *different* mode. The secondary references provide no nexus to link the bloodstream to the GI tract, or to the acute toxins removed from the bloodstream by the present method. Accordingly, the rejection of claims 27-29 as being obvious over the '918 patent in combination with the '563 and '871 patent should be withdrawn. For the same reasons set forth above, claims 3-6, 8, 12, 16, 18, 21, 22, 24, 25, and 36-39 also are patentable over the combination of cited references.

It is submitted that the claims are in a proper form and scope for allowance. An early and favorable action on the merits is respectfully solicited.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully submitted,

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